

Sleep: Perchance to Dream

Demystifying Medicine

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Characteristics of Sleep

- ❖ Absence of motion
- ❖ A characteristic posture
- ❖ Reduced response to sensory stimuli
- ❖ Immediately reversible



Research on Sleep

- ❖ Sleep disorders
- ❖ Effects of lack of sleep
- ❖ Need for sleep

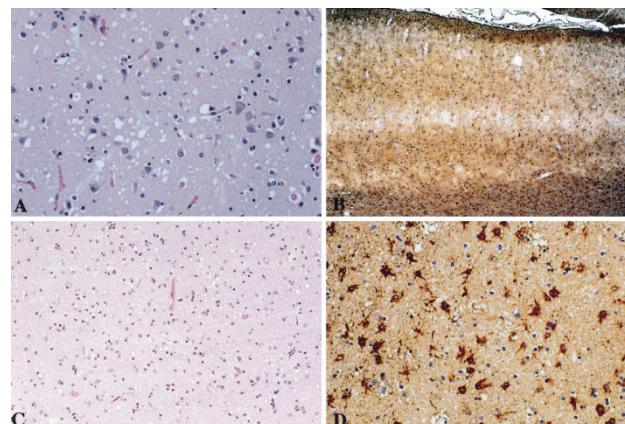
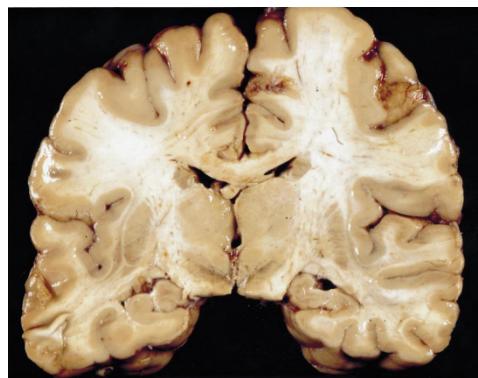


Disorders of Sleep

- ❖ **Insomnia**
- ❖ **Hypersomnia**
- ❖ **Restless leg syndrome**
- ❖ **Bruxism**
- ❖ **Sleep apnea**
- ❖ **Narcolepsy**

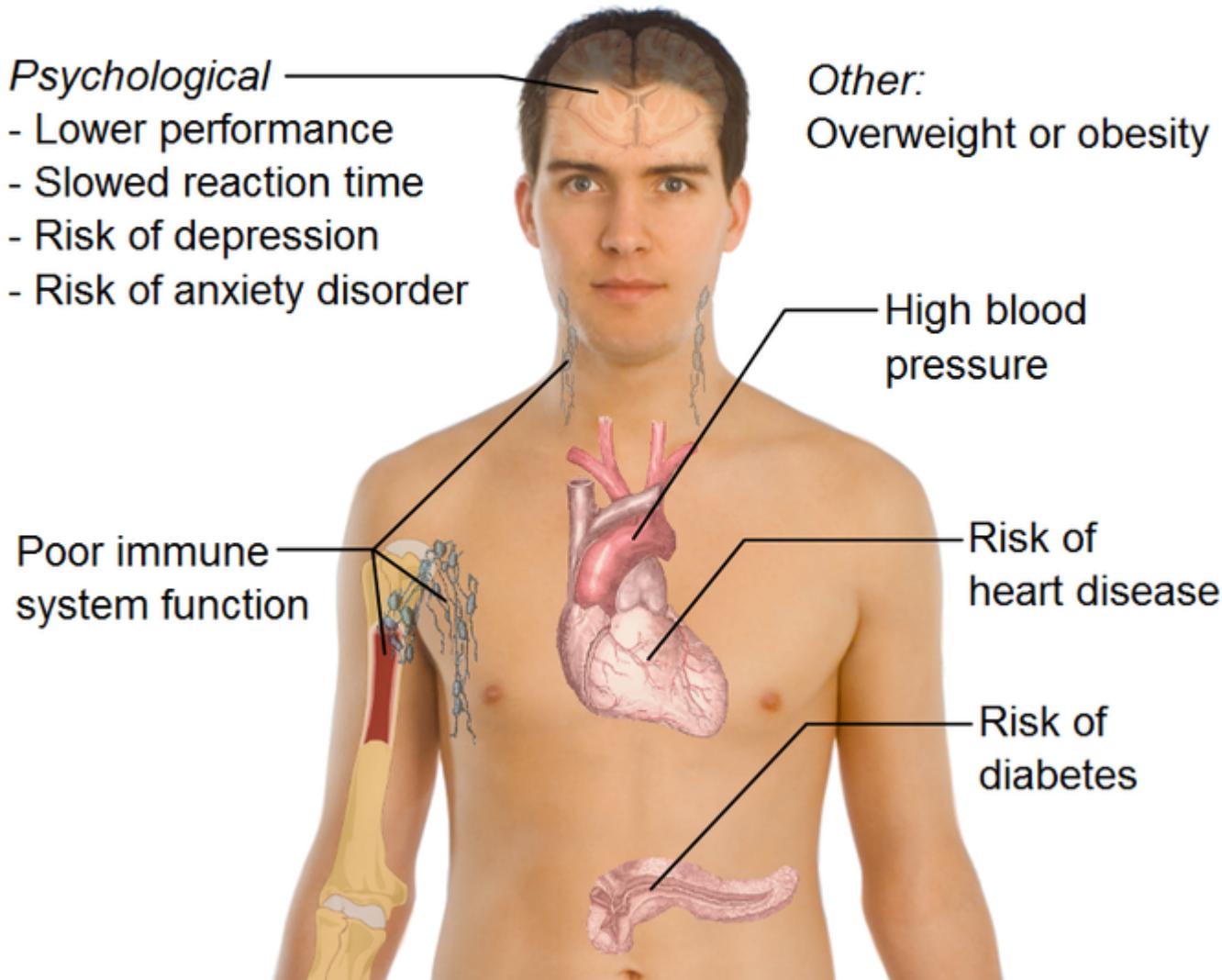
Fatal Familial Insomnia

- ❖ Progressive untreatable insomnia
- ❖ Prion disease
- ❖ Spongiform encephalopathy
- ❖ Lesions of the thalamus



(Almer et al. *Brain* 122:5-16, 1999)

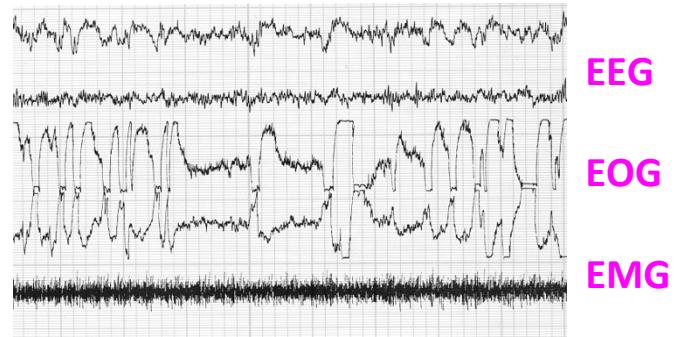
Effects of Sleep Deprivation



Polysomnography

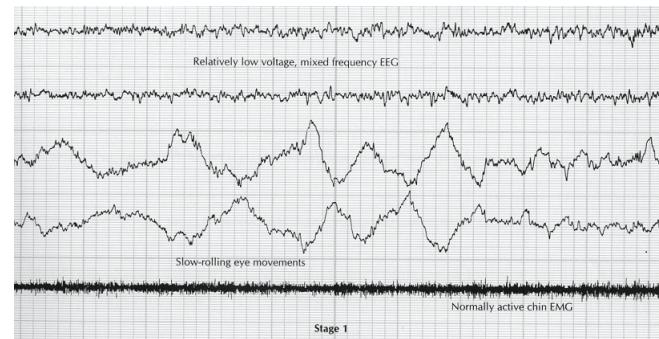
❖ Active wake

- ❖ EEG: High frequency
- ❖ EOG: Rapid eye movements
- ❖ EMG: Highest



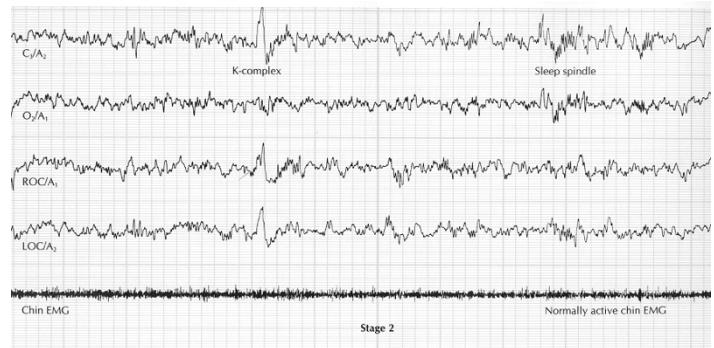
❖ Sleep Stage 1

- ❖ EEG: Low frequency
- ❖ EOG: Slow eye movements
- ❖ EMG: Medium



❖ Sleep Stage 2

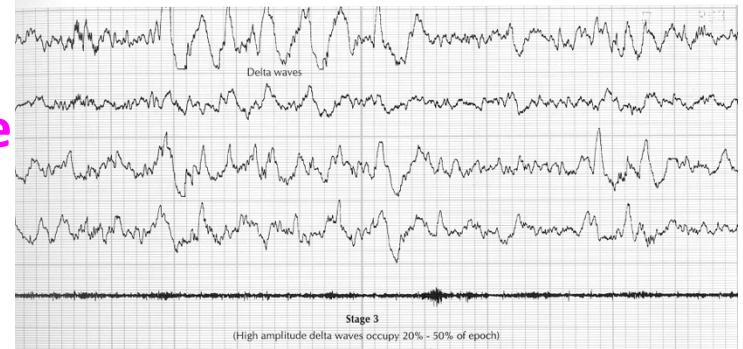
- ❖ EEG: Low frequency spindles & K-complexes
- ❖ EOG: No eye movements
- ❖ EMG: Medium



Polysomnography

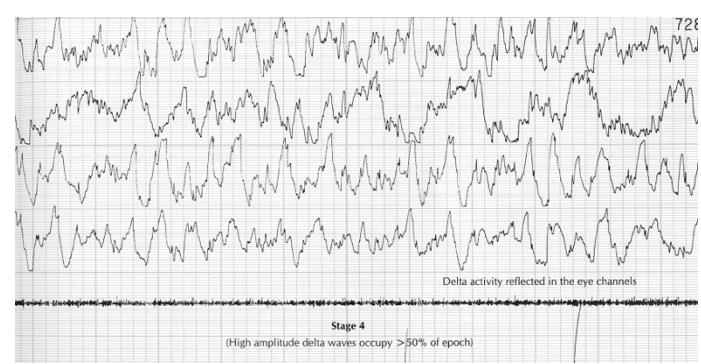
❖ Sleep Stage 3

- ❖ EEG: Lowest frequency, high amplitude
- ❖ EOG: No eye movements
- ❖ EMG: Low



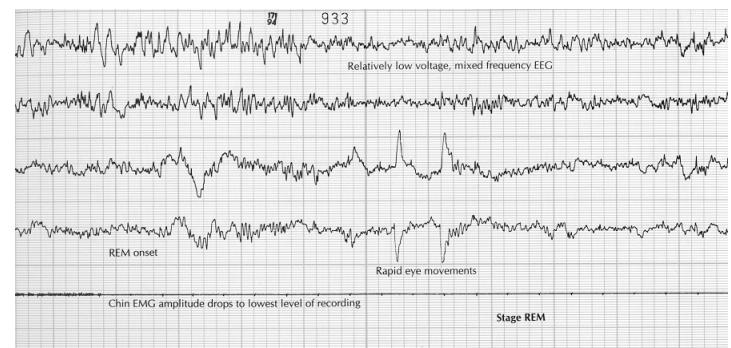
❖ Sleep Stage 4

- ❖ EEG: Same as Stage 3 with 50% Delta
- ❖ EOG: No eye movements
- ❖ EMG: Low



❖ Sleep REM

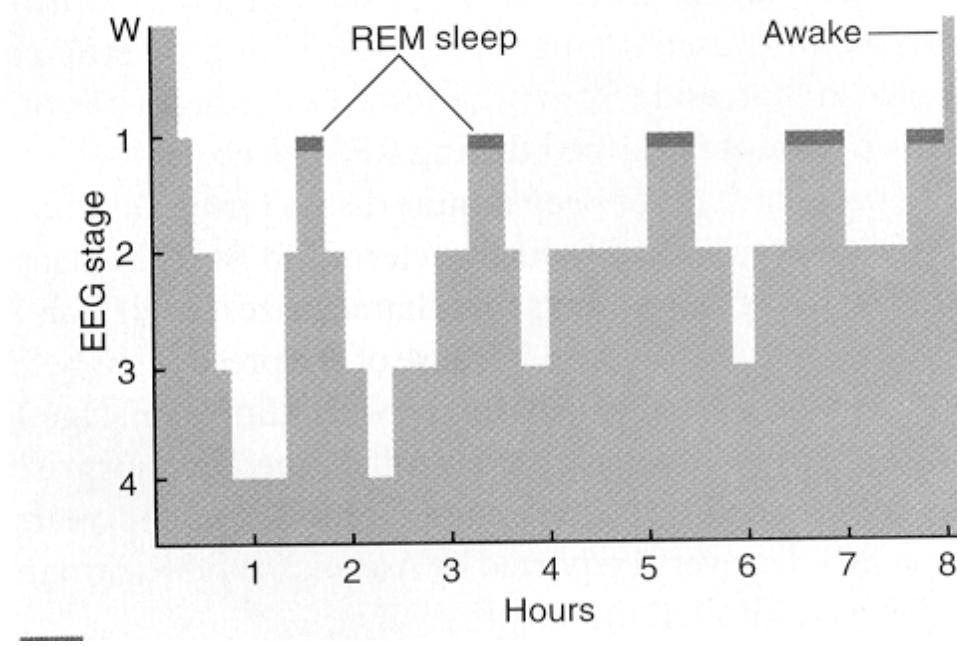
- ❖ EEG: Low frequency
- ❖ EOG: Rapid eye movements
- ❖ EMG: Lowest



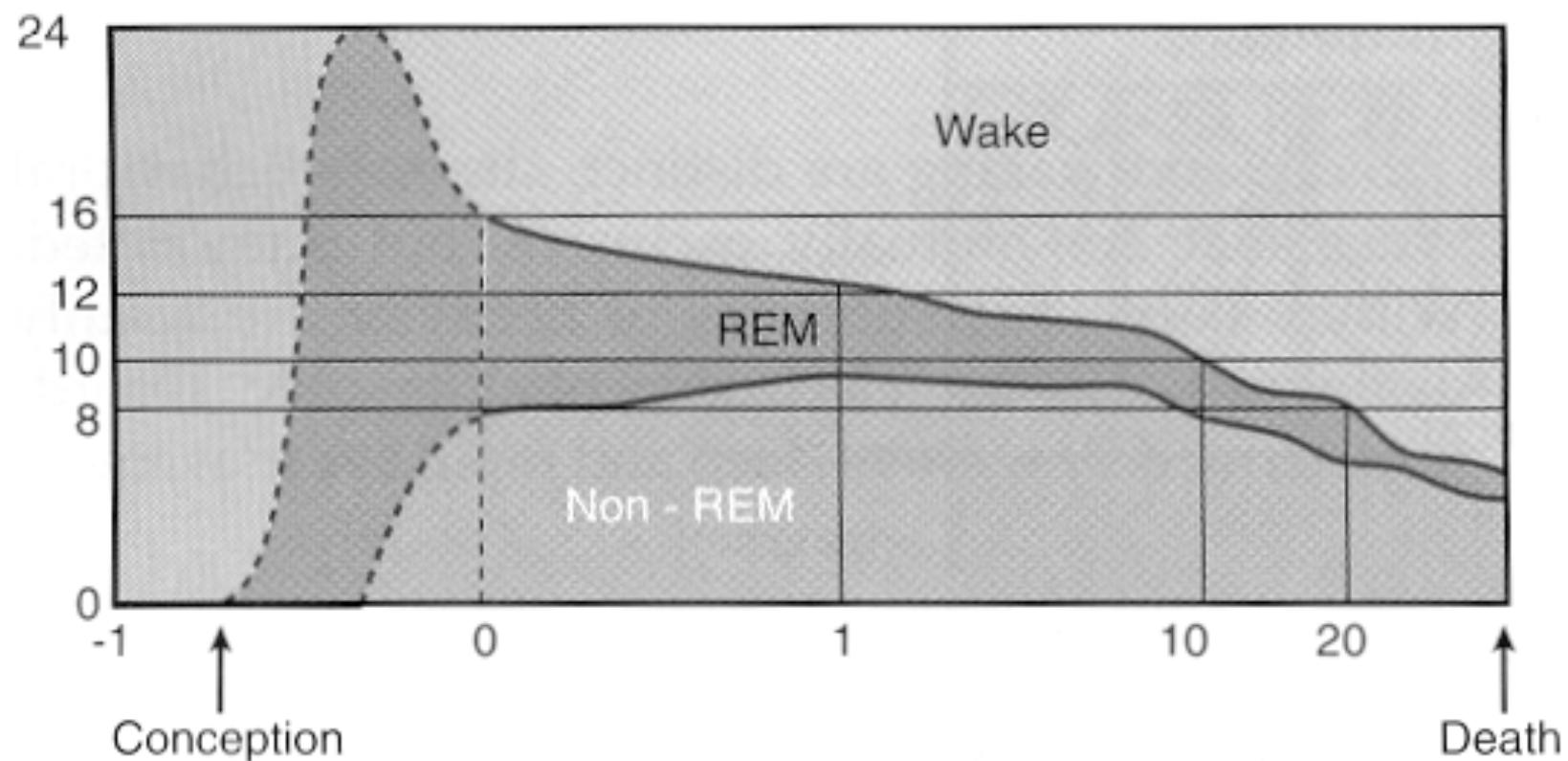
Summary of Sleep Stages

- ❖ Awake: desynchronized firing of neurons
- ❖ Non-REM Sleep: synchronized firing
- ❖ REM Sleep: desynchronized firing

Stages Over a Night of Sleep



Sleep Over a Lifetime



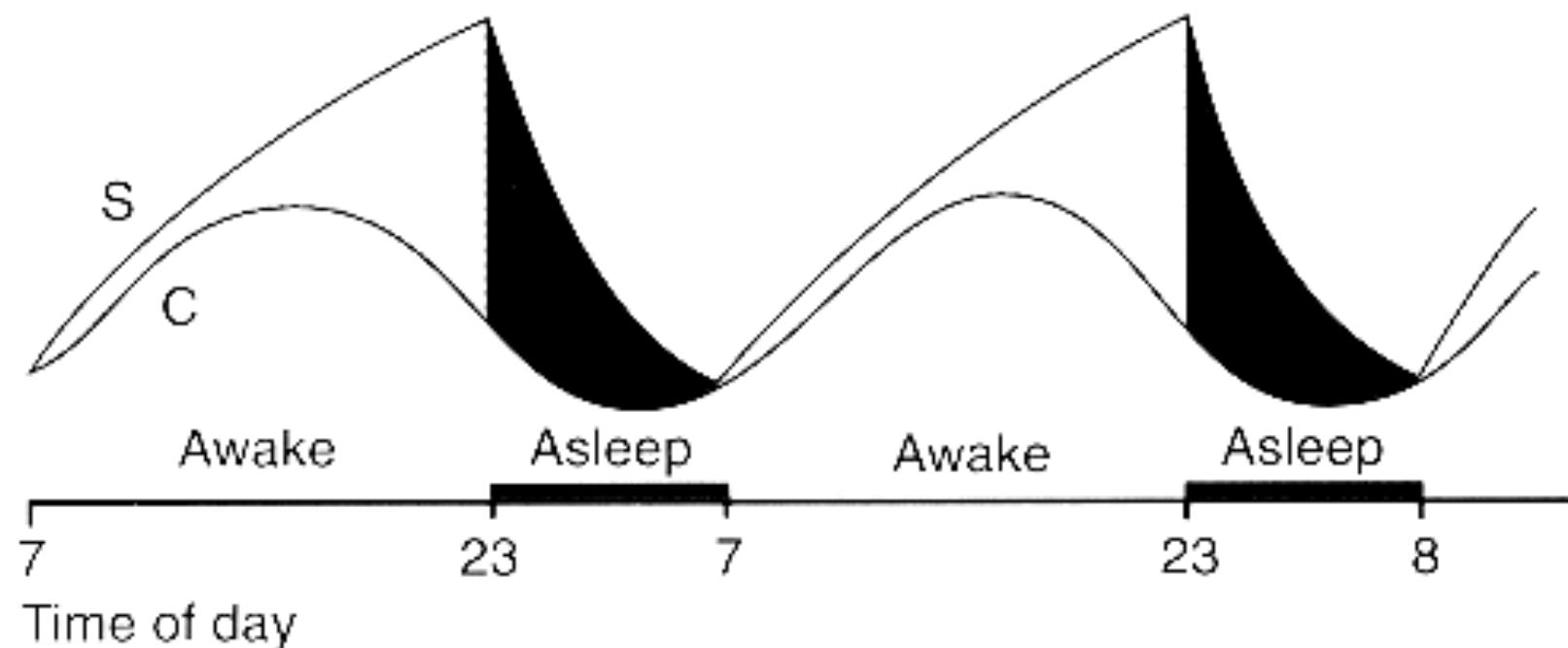
Drive for Sleep

- ❖ Process C
 - ❖ Circadian linked to the 24 h clock
- ❖ Process S
 - ❖ Homeostatic drive increases during wakefulness

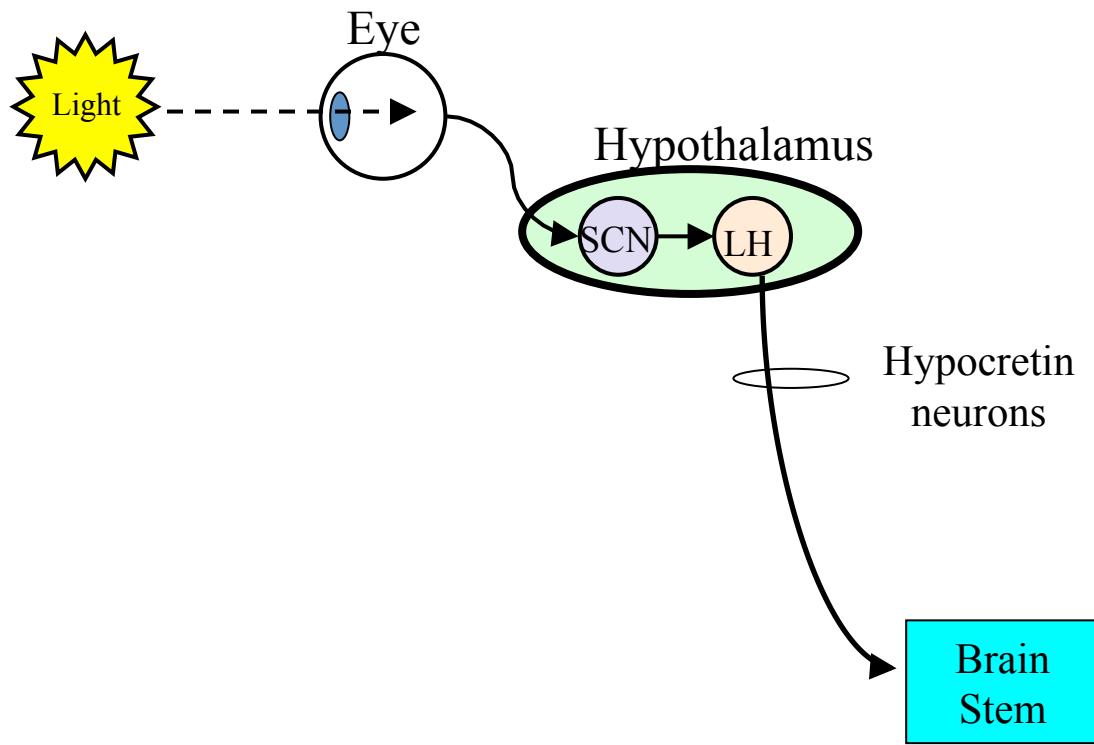
Two Process Model

A

Sleep/wake cycle



Circadian Rhythm and Sleep



Homeostatic Drive for Sleep

- ❖ Adenosine
 - ❖ Product of cellular energy metabolism
 - ❖ Accumulates during wakefulness
 - ❖ Acts as a neurotransmitter

Wakefulness

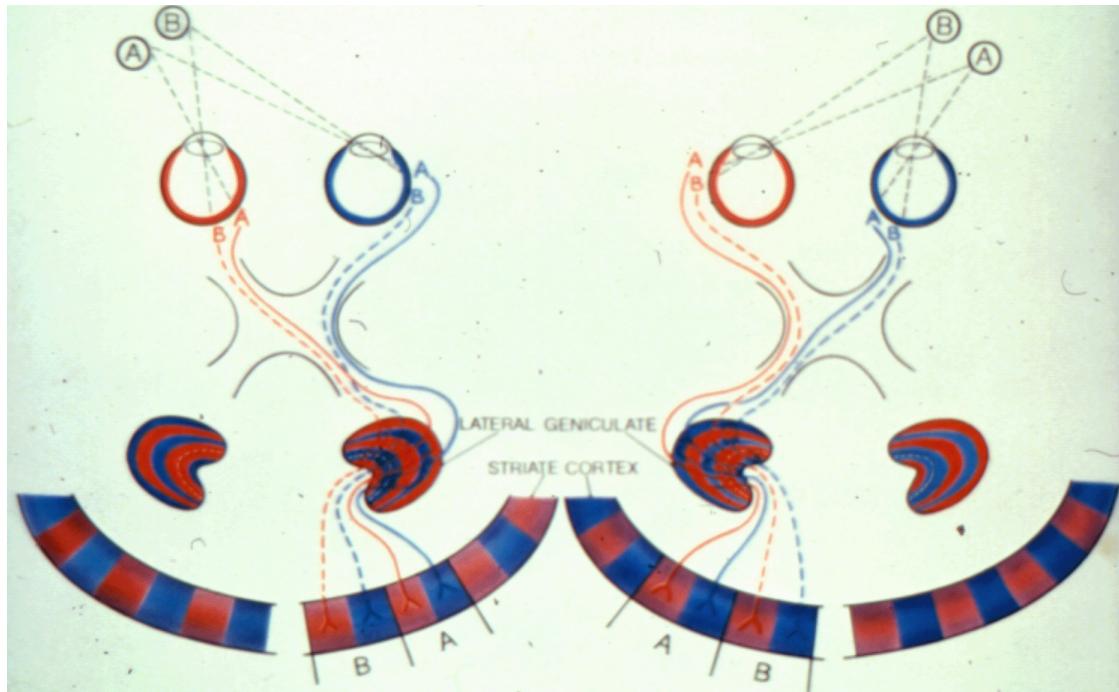
❖ Activating systems in the brain

- ❖ Reticular Activating System
 - ❖ Cholinergic
 - ❖ Projections from thalamus to cortex
- ❖ Locus Coeruleus
 - ❖ Noradrenergic projections to cortex and brain
 - ❖ Focus attention and enhance arousal
- ❖ Dorsal Raphe Nuclei
 - ❖ Widespread serotonergic projections
 - ❖ Maintain arousal

Possible Functions of Sleep

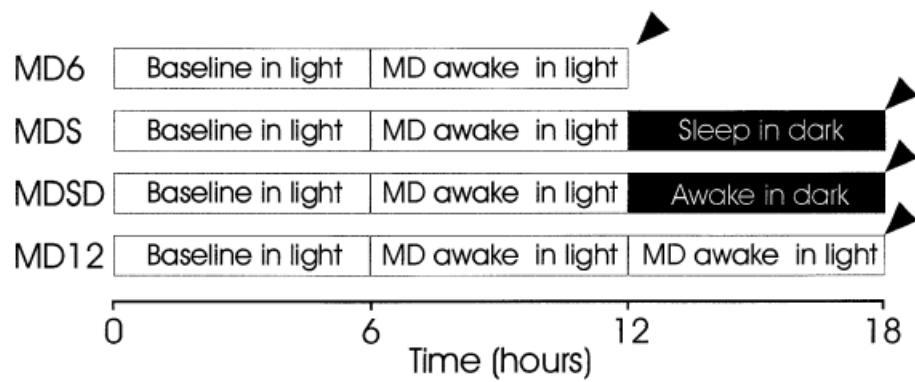
- ❖ Neuronal Detoxification
- ❖ Maintenance of nervous system structure
 - ❖ Protein synthesis
- ❖ Synaptic remodeling
 - ❖ Developmental plasticity
 - ❖ Learning & memory

Ocular Dominance Plasticity

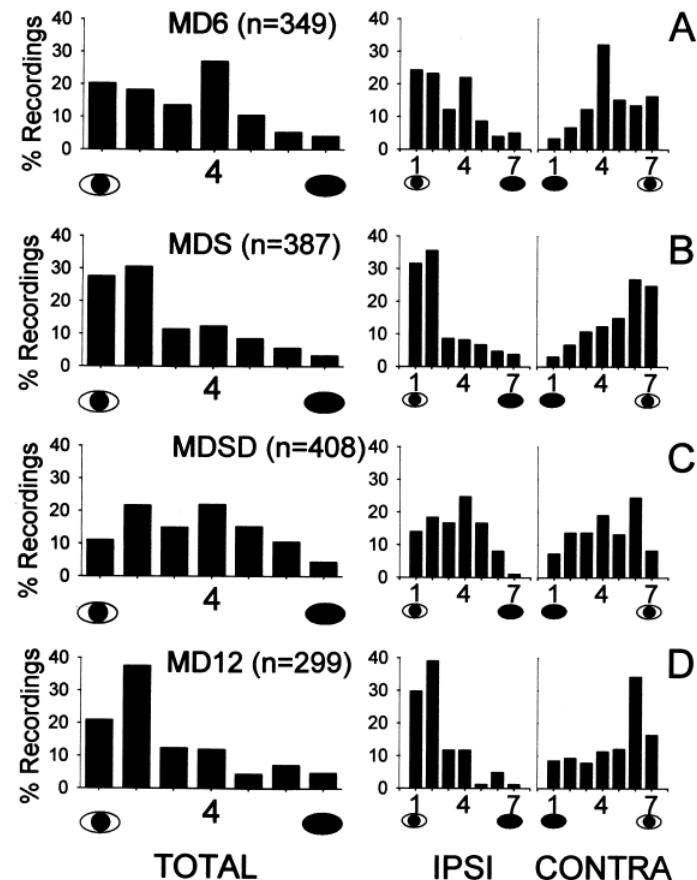


During development, monocular deprivation (MD) results in domination of the primary visual cortex by the open eye.

Sleep and Plasticity

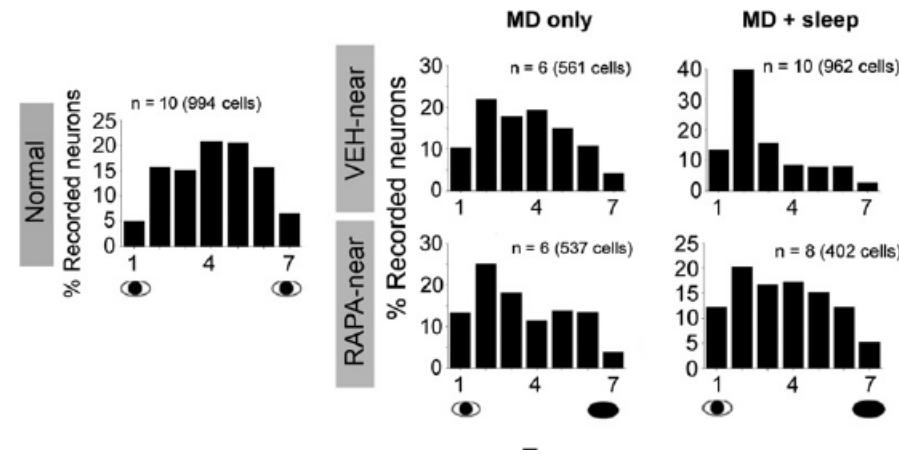
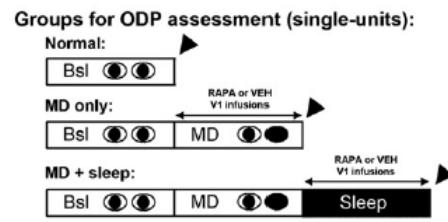


Sleep enhanced effects of a preceding period of MD on visual cortical responses (plasticity).



Consolidation of Plasticity During Sleep Protein Synthesis Dependent

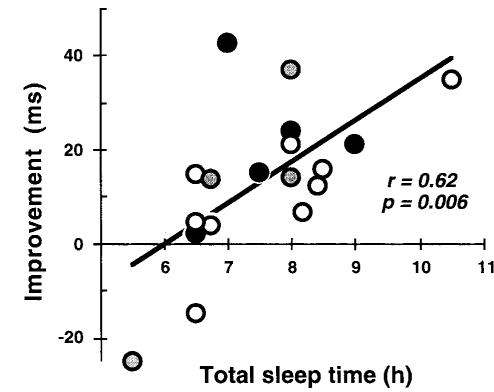
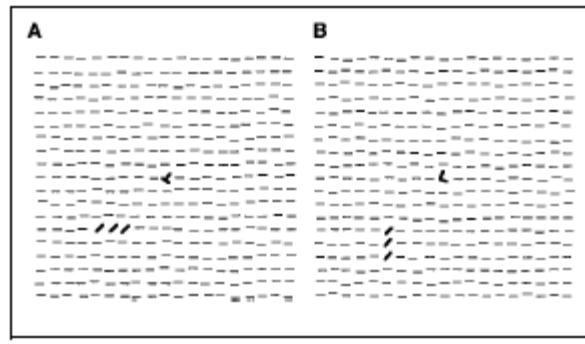
- ❖ mTOR pathway
- ❖ Change in ocular dominance blocked by rapamycin



Seibt et al, *Current Biology* 22:676-682, 2012.

Effect of Sleep on Memory Consolidation

❖ Texture Discrimination Task (TDT)



Stickgold et al, *J Cogn Neurosci* **12**:246-254, 2000.

Effect of Sleep on Protein Synthesis During Memory Consolidation

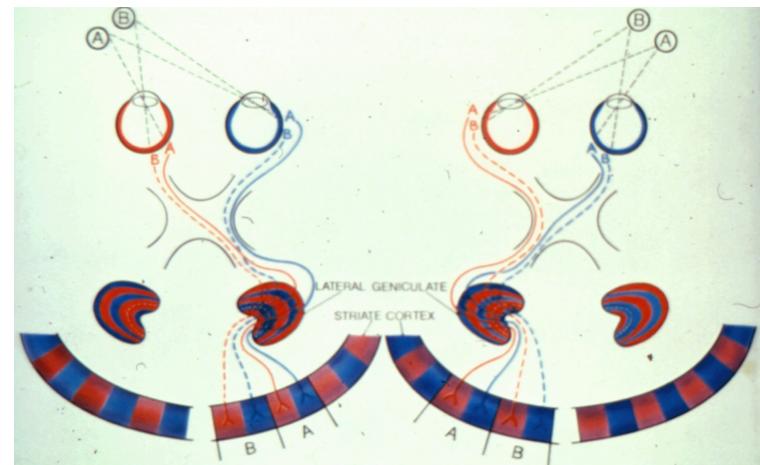
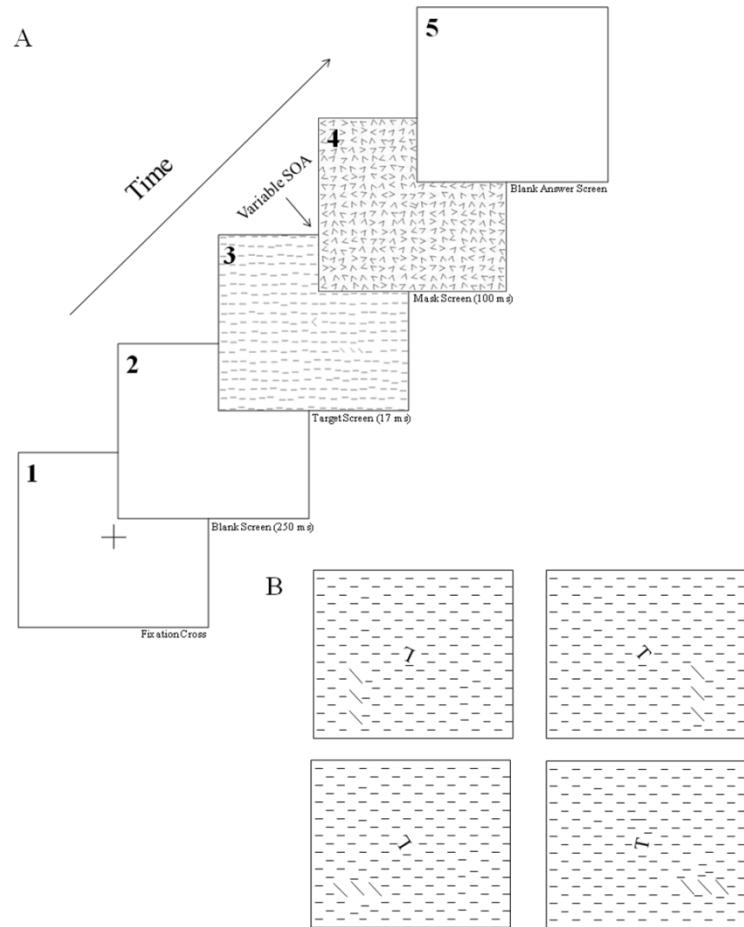
**Co-investigators: Tom Balkin, WRAIR; Dante Picchioni, NINDS;
Kathleen Schmidt, NIMH; Inna Loutaev, NIMH; Adriana Pavletic, NIMH**

Is the sleep-dependent improvement on performance on the TDT accompanied by changes in protein synthesis rates in parts of brain undergoing memory consolidation?

Effect of Sleep on Protein Synthesis During Memory Consolidation

- ❖ Healthy volunteers
 - ❖ 18-28 y
 - ❖ No neurological or psychiatric disease
 - ❖ No sleep issues
- ❖ Procedures
 - ❖ Sleep deprivation overnight
 - ❖ Trained on TDT
 - ❖ PET scan +/- sleep
 - ❖ Tested on TDT

Texture Discrimination Task

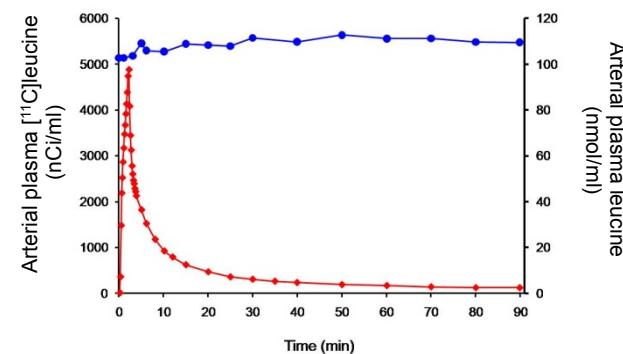


PET Measurement of rCPS *in Vivo* with L-[1-¹¹C]Leucine as Tracer

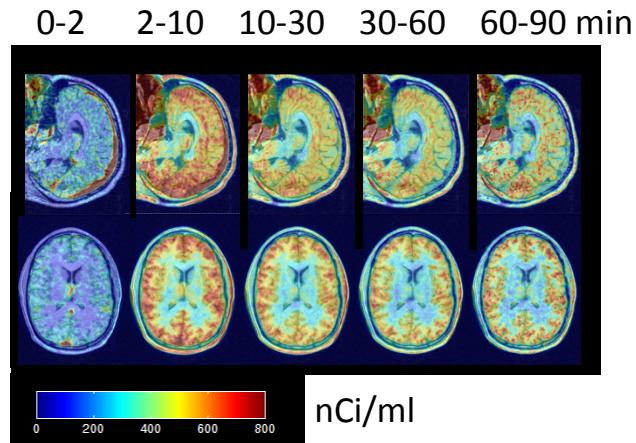
1. Awake or sleeping subject



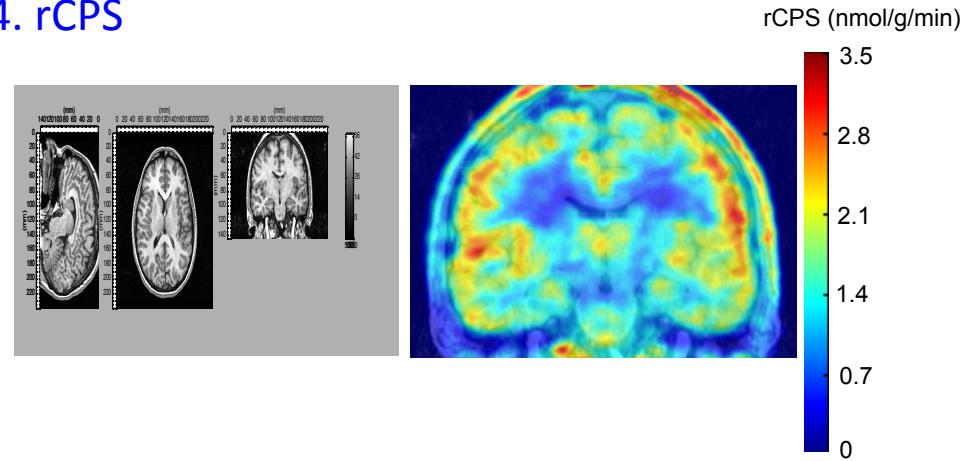
2. Time course of specific activity in plasma



3. Positron Emission Tomography

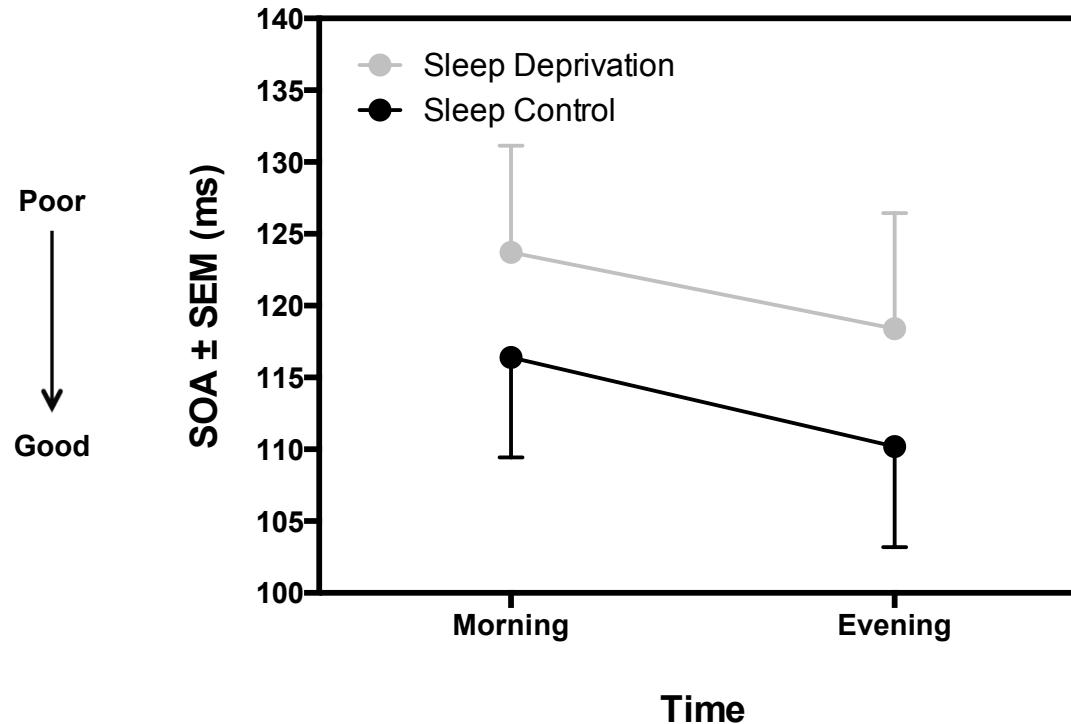


4. rCPS



Smith et al, *J Cereb Blood Flow & Metab* 25:629-640, 2005.

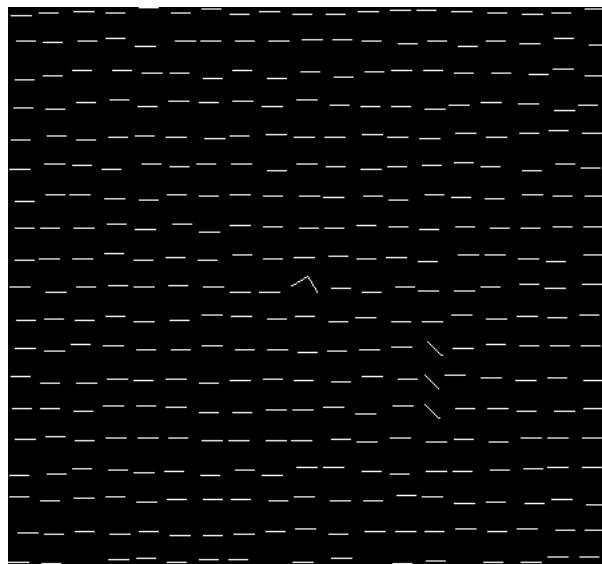
Effect of Prior Sleep Deprivation



Poor
↓
Good

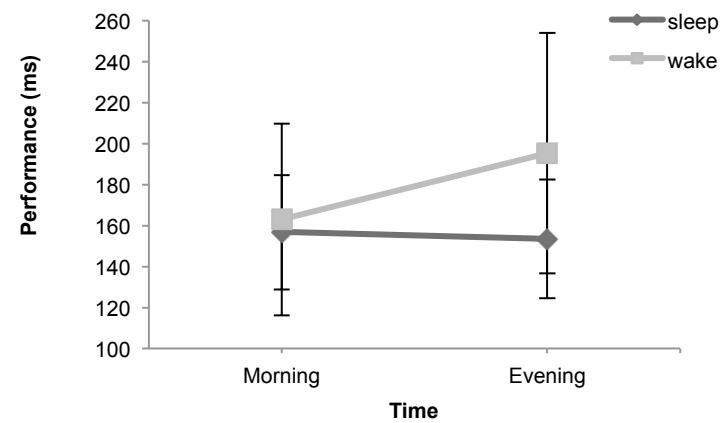
Effect of Nap on TDT Performance

Texture Discrimination Task

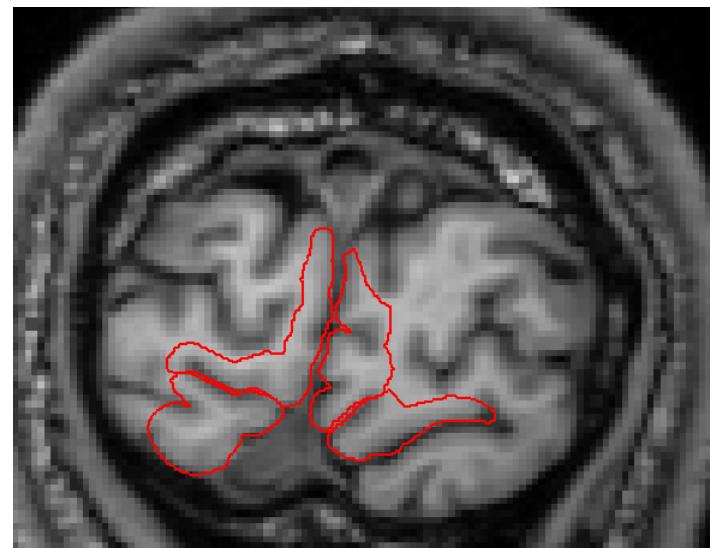


Poor
↓
Good

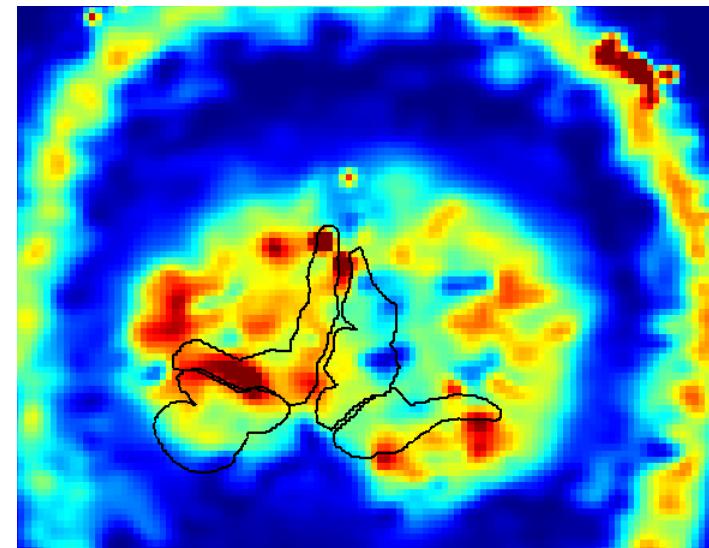
Performance



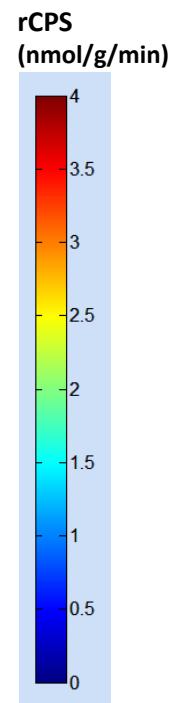
rCPS During Sleep



MRI



PET



Summary

- ❖ Sleep definition
- ❖ Sleep disorders
- ❖ Sleep drives
- ❖ Sleep & plasticity
- ❖ Sleep & memory
- ❖ Sleep & protein synthesis-dependent memory

